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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/027,201	12/20/2001	Stephen Quirk	1443.027US1	1416

21186 7590 08/08/2006

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EXAMINER	
COUNTS, GARY W	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 08/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/027,201	QUIRK, STEPHEN	
	Examiner	Art Unit	
	Gary W. Counts	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7,9-18 and 20-23* is/are pending in the application.

4a) Of the above claim(s) *23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7,9-18,20-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims

The amendment filed June 8, 2006 is acknowledged and has been entered.

Election/Restrictions

1. Newly submitted claim 23 directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Newly recited claim 23 requires a mixture of aspartic acid, glutamic acid, asparagines, arginine, and serine amino acids and claims 1-22 do not require this limitation. Further, claims 1-22 require a label covalently linked to the proteinoid microsphere and claim 23 does not require this limitation.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 23 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness..

4. Claims 1, 2, 5, 7, 9, 12-18 and 20-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lohrmann et al (US 6,193,953) in view of Steiner et al (US 4,925,673) and Kayyem et al (US 6,232,295).

Lohrmann et al disclose protein microparticles that can be comprised of chemically synthesized amino acid polymers (col 5, lines 40-57). Lohrmann et al disclose that the microparticles can comprise fluorines or I^{125} (radioisotope)(label) (col 15, lines 1-16). Lohrmann et al also disclose that the microparticles can comprise a targeting moiety such as an antibody linked to the microparticle (col 13, lines 27-29).

Lohrmann et al differ from the instant invention in failing to specifically teach that the protein microparticle is a proteinoid microparticle. Lohrmann et al also differ from the instant invention in failing to teach the label is linked to the proteinoid microsphere.

Steiner et al discloses proteinoid microspheres (microparticles). Steiner et al discloses that the proteinoid microspheres are man made condensation polymers produced by random or directed assembly of natural or synthetic amino acids. Steiner et al disclose methods of producing the microspheres by using heat to condense the amino acids (see examples). Steiner et al disclose a mixture of amino acids comprising an acidic amino acid and a basic amino acid (col 5, lines 27-51).

Kayyem et al disclose polymeric delivery vehicles that are tissue specific used in MRI applications. Kayyem et al disclose that a contrasting agent (label) is attached

(linked) to the polymeric delivery vehicle. Kayyem et al disclose that the label is covalently attached to the polymeric delivery vehicle. Kayyem et al disclose that this provides for a safe and effective means and for improved targeted delivery of contrast agents to specific cells or tissue (col 2-col 4) and allow for medical imaging.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to synthesize the protein microparticles of Lohrmann et al using condensed amino acids such as taught by Steiner et al because Lohrmann et al specifically teaches that the protein microparticles can be comprised of synthesized amino acid polymers and Steiner et al specifically teaches that proteinoid micropsheres are man made condensation polymers produced by random or directed assembly of synthetic amino acids. Therefore, one of ordinary skill in the art would have a reasonable expectation of success to form the protein microspheres of Lohrmann et al by condensing amino acids such as taught by Steiner et al. Therefore, the combination of Lohrmann et al and Steiner et al disclose proteinoid microspheres.

It also would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate attached labels as taught by Kayyem et al into the modified protein microparticles of Lohrmann et al because Lohrmann et al specifically disclose that their microparticles can be polymeric (col 5) and used in imaging applications. Further, Kayyem et al teaches that this provides for a safe and effective means and for improved targeted delivery of contrast agents to specific cells or tissue (col 2-col 4) and allow for medical imaging. Therefore, one of ordinary skill in the art

would have a reasonable expectation to attach labels as taught by Kayyem et al into the modified proteinoid microparticle of Lohrmann et al.

With respect to the recitation "and the proteinoid microsphere is stable in solution". Since the combination of the above references teach the same microspheres as recited. The modified microspheres of Lohrmann et al would be stable in solution.

With respect to claims 5 and 13-16 as recited in the instant claims. The claims are directed to intended use of the proteinoid microspheres and therefore are not given patentable weight. Further, since the combination of references disclose the claimed invention and the Applicant has not recited any structural differences over the prior art, the prior art is capable of performing the intended use.

5. Claims 3, 4, 10 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lohrmann et al in view of Steiner et al and Kayyem et al and further in view of Mathiowitz et al (US 5,271,961).

See above for the teachings of Lohrmann et al, Steiner et al and Kayyem et al.

Lohrmann et al., Steiner et al., and Kayyem et al differ from the instant invention in failing to teach the proteinoid microsphere is formed by thermal condensation of a mixture of amino acids in the presence of a cross linking agent.

Mathiowitz et al disclose protein microspheres that can be modified. Mathiowitz et al disclose that the modification of the protein can be done by cross-linking the protein using agents such as glutataldehyde (col 6, lines 51-62). Mathiowitz et al disclose that such modifications provides a protein having enhanced or altered thermal

stability, surface reactivity, molecular weight, charge and resistance to proteases (col 5, lines 50-56).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate cross-linking as taught by Mathiowitz et al into the modified microspheres of Lohrmann et al because Mathiowitz et al shows that such modifications provides a protein having enhanced or altered thermal stability, surface reactivity, molecular weight, charge and resistance to proteases.

Response to Arguments

6. Applicant's arguments filed June 8, 2006 have been fully considered but they are not persuasive.

Applicant argues that the combination of Lohrmann, Steiner and Kayyem fails to disclose labeled proteinoid microspheres comprising a mixture of amino acids that are thermally condensed. This is not found persuasive because Lohrmann et al specifically teaches that the protein microspheres can be comprised of chemically synthesized amino acid polymers and Steiner et al disclose producing proteinoid microspheres (microparticles) by condensing amino acids using heat (thermal). Applicant argues that any teachings on delivery vehicles and microspheres composed of proteins are irreleveant because the chemical and physical properties of such protein microspheres are different from those of the present invention. Applicant states that for example, microspheres made from proteins are held together by standard peptidyl bonds, hereas microspheres made from thermally-condensed amino acids can have a variety of bonds between their side chain moieties as well as their amino acid and carboxylate moieties.

This is not found persuasive because the combination of Lohramman, Steiner and Kayyem teach the same proteionoid microspheres as currently claimed and thus would have the same bonds. Further, there is no recitation of bonds between the side chain moieties or carboxylate moieties recited in the current claims.

Applicant argues that the Steiner reference explicitly focuses on release of a pharmacological agents rather than a retention of a label in the proteinoid microspheres. Applicant argues that one of skill in the art would not be motivated to modify or combine the teachings of Lohrmann on stabilized protein microparticles with the teachings of Steiner on unstable proteinoid microspheres. This is not found persuasive because as stated above and in the previous office action Lohrmann et al specifically teaches that the protein microparticles can be comprised of synthesized amino acid polymers and Steiner et al specifically teaches that proteinoid micropsheres are man made condensation polymers produced by random or directed assembly of synthetic amino acids. Applicant further argues that there is no evidence of record that the proteinoid microspheres of Steiner have properties similar to the protein microspheres of Lohrmann hat would suggest their interchageability. This is not found persuasive because as stated above Lohrmann et al specifically teaches that the protein microspheres can be comprised of synthetic amino acids and Steiner specifically teaches that proteinoid micropsheres are man made condensation polymers produced by random or directed assembly of synthetic amino acids. Applicant further argues the combination of references does not disclose that proteinoid microspheres would be sufficiently stable in solution and under a varity of pH and other conditions to retain the

integrity of the microsphere and the label. This is not found persuasive because "stable in solution" " is a characteristic of the proteinoid microspheres and since the combination of references teach the same proteinoid microspheres as claimed, the microsphere of the combined references would be stable in solution. Also, in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., under a variety of pH and other conditions to retain the integrity of the microsphere and the label) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Applicant states that Steiner discloses only unstable proteinoid microspheres that readily release pharmacological agents. This is not found persuasive because Applicant has not provided evidence that the proteinoid microspheres are unstable. Further, Applicant has not provided anything over that prior art of record that differentiates their proteinoid microsphere from that of the combination of Lohrmann, Steiner and Kayyem. Further, Applicant own proteinoid microsphere as claimed comprises condensed amino acids the same as disclosed by Steiner. Therefore, absent evidence to the contrary it appears that the proteinoid microspheres are as stable as Applicant's. Applicant further argues that simple substitution of the proteinoid microspheres of Steiner for the protein microcapsules of Lohrmann would not successfully generate the present invention. This is not found persuasive because as stated in the previous office action the

Examiner has not stated substituting the particles of Lohrmann et al with the proteinoid microspheres of Steiner (see 103 obviousness rejection above).

Applicant argues that Mathiowitz is limited to methods for making protein microspheres by solvent evaporation of a solution of proteins (not amino acids). This is not found persuasive because Mathiowitz et al clearly teaches that the protein can by modified by crosslinking amino acids (col 6, lines 54-62). Further, proteinoids are thermal protein polymers containing amino acids and proteins are polymers of amino acids (5,679,377, col. 1, lines 25-50). Applicant further argues that Mathiowitz emphasizes that the protein microspheres are made under gentle conditions and teaches that the proteins are treated with crosslinking agent prior to formation of protein microspheres. This is not found persuasive because the current claims are not directed to methods of making but rather are directed to the proteinoid microspheres thus the argument is not on point. Applicant further states that mere mention of a cross-linker reference does not mean that one of skill in the art would necessarily know how or why to use the cross-linking agent and that there must be some teaching in the cited references to motivate one of skill in the art to make and use the invention. This is not found persuasive because as stated above the art of proteinoids and protein microspheres is analogus art because, proteinoids are thermal protein polymers containing amino acids and proteins are polymers of amino acids and Mathiowitz et al specifically teaches that cross-linking provides for a protein having enhanced or altered thermal stability and surface reactivity thus motivation is clearly provided.

Applicant's argues that there is no motivation to modify the teachings of Steiner on unstable proteinoid microspheres by addition the crosslinking agent disclosed in Mathiowitz. This is not found persuasive because the rejection is not based on the mere combination of Steiner and Mathiowitz but rather is based on the combination of Primary reference Lohrmann in view of Steiner et al and Kayyem et al and further in view of Mathiowitz et al thus it appears that Applicant is arguing the references individually. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant argues that Lohrmann and Steiner fail to disclose that proteinoid microspheres would be sufficiently stable under a variety of pH and other conditions to retain an encapsulated label, and that Mathiowitz not only provides no methods for forming microspheres in the presence of crosslinking agent but actually states that one of skill should not form microspheres in the presence of a crosslinking agent, the skilled artisan could not reasonable expect to successfully make the present invention. This is not found persuasive because (1) in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., under a variety of pH and other conditions to retain the integrity of the microsphere and the label) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from

the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). (2) the claims are not directed to methods of making the microparticles but rather are directed to the proteinoid microspheres and further as stated above Mathiowitz clearly teaches that the protein can by modified by crosslinking amino acids.

Conclusion

7. No claims are allowed.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Gary Counts
Examiner
Art Unit 1641
July 26, 2006

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